

Claims

1. A kit for treatment of a subject which kit comprises
in a first container a composition comprising delivery vehicles stably associated with at least one first therapeutic agent;
in a second container a second composition comprising delivery vehicles stably associated with at least a second therapeutic agent;
wherein the delivery vehicles in said first and second compositions are coordinated with respect to pharmacokinetic behavior; and
wherein said kit further contains instructions for administering said first and second composition at ratios of said first and second therapeutic agent that are non-antagonistic and/or wherein the amounts of said first and second compositions in said containers is proportional to a ratio of said first and second therapeutic agent that is non-antagonistic and/or said containers are calibrated to dispense amounts of said first and second composition wherein the ratio of first and second therapeutic agents is non-antagonistic.
2. The kit of claim 1, wherein the containers are syringes.
3. The kit of claim 1 or 2, wherein said agents are antineoplastic agents.
4. The kit of any of claims 1-3, wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range where $> 1\%$ of relevant cells are affected ($f_a > 0.01$) in an *in vitro* assay for cytotoxicity.
5. The kit of claim 4, wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 10-90% of the cells are affected ($f_a = 0.1-0.9$) in said *in vitro* assay.
6. The kit of claim 5, wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 20-80% of the cells are affected ($f_a = 0.2-0.8$) in said *in vitro* assay.
7. The kit of claim 6, wherein said non-antagonistic effect is exhibited over at least 20% of the concentration range such that 20-80% of the cells are affected in said *in vitro* assay.

8. The kit of any of claims 1-7, wherein said delivery vehicles have a mean diameter of between 4.5 and 500 nm.

9. The kit of claim 8, wherein said vehicles have a mean diameter of less than 250 nm.

10. The kit of any of claims 1-9, wherein said delivery vehicles comprise
liposomes, and/or
lipid micelles, and/or
block copolymer micelles, and/or
microparticles, and/or
nanoparticles, and/or
polymer lipid hybrid systems, and/or
derivatized single chain polymers.

11. The kit of any of claims 1-10, wherein at least one of the agents is selected from the group consisting of a DNA damaging agent, a DNA repair inhibitor, a topoisomerase I inhibitor, a topoisomerase II inhibitor, a cell checkpoint inhibitor, a CDK inhibitor, a receptor tyrosine kinase inhibitor, a cytotoxic agent, an apoptosis inducing agent, an antimetabolite, a cell cycle control inhibitor, a therapeutic lipid, a telomerase inhibitor, an anti-angiogenic agent, a mitochondrial poison, a signal transduction inhibitor and an immunoagent.

12. The kit of any of claims 1-10, wherein the first agent is a cytotoxic agent and the second agent is a cell-cycle inhibitor, or

wherein the first agent is a DNA damaging agent and the second agent is a DNA repair inhibitor, or

wherein the first agent is a topoisomerase I inhibitor and the second agent is a S/G₂- or a G₂/M-checkpoint inhibitor, or

wherein the first agent is a G₁/S checkpoint inhibitor or a cyclin-dependent kinase inhibitor and the second agent is a G₂/M checkpoint inhibitor, or

wherein the first agent is a receptor kinase inhibitor and the second agent is a cytotoxic agent, or

wherein the first agent is an apoptosis-inducing agent and the second agent is a cytotoxic agent, or

wherein the first agent is an apoptosis-inducing agent and the second agent is a cell-cycle control agent, or

wherein the first agent is a telomerase inhibitor and the second agent is a cell-cycle control inhibitor, or

wherein the first and second agents are antimetabolites, or

wherein the first and second agents are cytotoxic agents, or

wherein the first agent is a therapeutic lipid and the second agent is a cytotoxic agent, or

wherein the first agent is a topoisomerase I inhibitor and the second agent is a DNA repair inhibitor, or

wherein the apoptosis-inducing agent is a serine-containing lipid.

13. The kit of any of claims 1-10, wherein the first agent is irinotecan and the second agent is 5-FU or FUDR, or

wherein the first agent is cisplatin (or carboplatin) and the second agent is 5-FU or FUDR, or

wherein the first agent is idarubicin and the second agent is AraC or FUDR, or

wherein the first agent is oxaliplatin and the second agent is 5-FU or FUDR, or

wherein the first agent is irinotecan and the second agent is cisplatin (or carboplatin), or

wherein the first agent is gemcitabine and the second agent is cisplatin (or carboplatin), or

wherein the first agent is methotrexate and the second agent is 5-FU or FUDR, or

wherein the first agent is paclitaxel and the second agent is cisplatin (or carboplatin), or

wherein the first agent is etoposide and the second agent is cisplatin (or carboplatin), or

wherein the first agent is docetaxel or paclitaxel and the second agent is doxorubicin, or

wherein the first agent is doxorubicin and the second agent is vinorelbine, or

wherein the first agent is carboplatin and the second agent is vinorelbine, or

wherein the first agent is 5-FU or FUDR and the second agent is gemcitabine.

14. A method to treat a disease condition in a subject which method comprises administering to a subject in need of such treatment a therapeutically effective amount of a first

composition comprising delivery vehicles stably associated with at least a first therapeutic agent and a second composition comprising delivery vehicles stably associated with at least a second therapeutic agent,

wherein the delivery vehicles in said first and second composition are coordinated with respect to pharmacokinetics; and

wherein said administering is at a ratio of first therapeutic agent to second therapeutic agent that is non-antagonistic.

15. The method of claim 14, wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 1%-99% of the cells are affected ($f_a = 0.01-0.99$) in an *in vitro* assay for cytotoxicity or cytostasis.

16. The method of claim 15, wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 10-90% of the cells are affected ($f_a = 0.1-0.9$) in an *in vitro* assay for cytotoxicity or cytostasis.

17. The method of claim 16, wherein said non-antagonistic effect is exhibited over at least 5% of the concentration range such that 20-80% of the cells are affected ($f_a = 0.2-0.8$) in an *in vitro* assay for cytotoxicity or cytostasis.

18. The method of claim 17, wherein said synergistic effect is exhibited over at least 20% of the concentration range such that 20-80% of the cells are affected in an *in vitro* assay for cytotoxicity or cytostasis.

19. The method of any of claims 14-18, wherein said delivery vehicles have a mean diameter of between 4.5 and 500 nm.

20. The method of any of claims 14-18, wherein said vehicles have a mean diameter of less than 250 nm.

21. The method of any of claims 14-18, wherein said delivery vehicles comprise liposomes, and/or lipid micelles, and/or block copolymer micelles, and/or microparticles, and/or nanoparticles, and/or polymer lipid hybrid systems, and/or derivatized single chain polymers.
22. The method of any of claims 14-21, wherein at least one of the agents is selected from the group consisting of a DNA damaging agent, a DNA repair inhibitor, a topoisomerase I inhibitor, a topoisomerase II inhibitor, a cell checkpoint inhibitor, a CDK inhibitor, a receptor tyrosine kinase inhibitor, a cytotoxic agent, an apoptosis inducing agent, an antimetabolite, a cell cycle control inhibitor, a therapeutic lipid, a telomerase inhibitor, an anti-angiogenic agent, a mitochondrial poison, a signal transduction inhibitor and an immunoagent.
23. The method of any of claims 14-21, wherein the first agent is a cytotoxic agent and the second agent is a cell-cycle inhibitor, or
wherein the first agent is a DNA damaging agent and the second agent is a DNA repair inhibitor, or
wherein the first agent is a topoisomerase I inhibitor and the second agent is a S/G₂- or a G₂/M-checkpoint inhibitor, or
wherein the first agent is a G₁/S checkpoint inhibitor or a cyclin-dependent kinase inhibitor and the second agent is a G₂/M checkpoint inhibitor, or
wherein the first agent is a receptor kinase inhibitor and the second agent is a cytotoxic agent, or
wherein the first agent is an apoptosis-inducing agent and the second agent is a cytotoxic agent, or
wherein the first agent is an apoptosis-inducing agent and the second agent is a cell-cycle control agent, or
wherein the first agent is a telomerase inhibitor and the second agent is a cell-cycle control inhibitor, or

wherein the first and second agents are antimetabolites, or
wherein the first and second agents are cytotoxic agents, or
wherein the first agent is a therapeutic lipid and the second agent is a cytotoxic agent, or
wherein the first agent is a topoisomerase I inhibitor and the second agent is a DNA repair inhibitor, or
wherein the apoptosis-inducing agent is a serine-containing lipid.

24. The method of any of claims 14-21, wherein the first agent is irinotecan and the second agent is 5-FU or FUDR, or

wherein the first agent is cisplatin (or carboplatin) and the second agent is 5-FU or FUDR, or

wherein the first agent is idarubicin and the second agent is AraC or FUDR, or
wherein the first agent is oxaliplatin and the second agent is 5-FU or FUDR, or
wherein the first agent is irinotecan and the second agent is cisplatin (or carboplatin), or
wherein the first agent is gemcitabine and the second agent is cisplatin (or carboplatin), or

wherein the first agent is methotrexate and the second agent is 5-FU or FUDR, or
wherein the first agent is paclitaxel and the second agent is cisplatin (or carboplatin), or
wherein the first agent is etoposide and the second agent is cisplatin (or carboplatin), or
wherein the first agent is docetaxel or paclitaxel and the second agent is doxorubicin, or
wherein the first agent is doxorubicin and the second agent is vinorelbine, or
wherein the first agent is carboplatin and the second agent is vinorelbine, or
wherein the first agent is 5-FU or FUDR and the second agent is gemcitabine.